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RECEIVED
TECH CENTER 1600/2900
AUG 08 2003

July 31, 2003

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Re: U.S. Patent Application No.: 10/076934
For: *AGENTS THAT SPECIFICALLY BLOCK CD28-MEDIATED SIGNALING AND USES THEREOF*
Inventors: O'Hara, Jr., Richard M. *et al.*
Filed: February 15, 2002
Our Ref. No.: GNN-028

Dear Sir:

I enclose herewith for filing in the above-identified application the following:

1. Supplemental Information Disclosure Statement;
2. PTO Form 1449;
3. Copies of references cited in PTO Form 1449 (8);
4. A copy of the International Search Report; and
5. A Return Postcard.

No additional costs are believed to be due in connection with the filing of this Supplemental Information Disclosure Statement. However, please charge any other necessary fees due in connection with the enclosed statement to our Deposit Order Account No. 12-0080. For this purpose, a duplicate of this sheet is attached.

I hereby certify that this correspondence is deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on:

July 31, 2003
Date

Megan E. Williams, Esq., Registration No. 43,270

Respectfully submitted,
LAHIVE & COCKFIELD, LLP

Megan E. Williams, Esq.
Registration No. 43,270
Attorney for Applicants



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RECEIVED
AUG 08 2003
TECH CENTER 1600/2900

In re the application of: Ohara, Jr., Richard M. *et al.*

Serial No.: 10/076934

Filed: February 15, 2002

For: *AGENTS THAT SPECIFICALLY BLOCK CD28-MEDIATED SIGNALING AND USES THEREFOR*

Attorney Docket No.: GNN-028

Group Art Unit: 1614

Examiner: Not Yet Assigned

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Certificate of First Class Mailing (37 CFR §1.8(a))

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on the date set forth below.

July 31, 2003

Date of Signature and of Mail Deposit

By:


Megan E. Williams, Esq.
Reg. No. 43,270
Attorney for Applicants

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Dear Sir:

Applicants and their Attorney have become aware of the following publications and information, cited in an International Search Report mailed March 31, 2003 during the prosecution of PCT/US02/04772 which corresponds to the above referenced application. In accordance with 37 CFR §1.97, Applicants hereby submit these publications for the Examiner's consideration. These publications are cited on the enclosed PTO Form 1449, and a copy of the Report and each publication cited thereon are enclosed as well.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other

relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, the Applicants understand that the Examiner will make an independent evaluation of the cited publications.

Under 37 CFR § 1.97(b)(3), no additional costs are believed to be due in connection with the filing of this disclosure. If, however, a first Office Action on the merits issues in this application bearing a mailing date prior to the date of this Information Disclosure Statement, please charge the appropriate fee as required under 37 CFR §1.17(p) to our Deposit Order Account No. 12-0080.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP



Megan E. Williams, Esq.
Registration No. 43,270
Attorney for Applicants

28 State Street
Boston, MA 02109
(617) 227-7400

Date: July 31, 2003

AEM/MEW/JXM/kjr
Enclosures

APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTY DOCKET NO GNN-028	SERIAL NO. 10/076934
LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)				APPLICANT O'Hara, Jr., Richard M. et al.	
				FILING DATE February 15, 2002	GROUP 1614

O I P E J C
AUG 04 2003
PATENT & TRADEMARK OFFICE

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
C1	WO 92/00092 A1	01/92	WO			
C2	WO 92/15671 A1	09/92	WO			
C3	WO 94/28912 A1	12/94	WO			
C4	WO 98/56401 A1	12/98	WO			
C5	WO 02/051871 A2, A3	07/02	WO			Abstract Only

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

C6	Perrin, P.J. et al. "Blockade of CD28 during in vitro activation of encephalitogenic T cells or after disease onset ameliorates experimental autoimmune encephalomyelitis," <i>Journal of Immunology</i> 163(3):1704-10 (Aug. 1999).
C7	Silver, P.B. et al. "Blockade of costimulation through B7/CD28 inhibits experimental autoimmune uveoretinitis, but does not induce long-term tolerance," <i>Journal of Immunology</i> 165(9):5041-7 (Nov. 2000).
C8	Tan, P. et al. "Humanization of an anti-CD28 antibody using germline human antibody sequences," <i>Blood</i> 96(11):31A (Nov. 2000).

RECEIVED
AUG 08 2003
TECH CENTER 1600/2900

Examiner	Date Considered
*EXAMINER:	Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

VJ

PCT

To:
LAHIVE & COCKFIELD, LLP
 Attn. Mandragouras, Amy E.
 28 State Street
 Boston, MA 02109
 UNITED STATES OF AMERICA

DOCKETED

*copy 31.03.2003-Amend Search
after*

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference GNN-028PC	Date of mailing <i>(day/month/year)</i> 31/03/2003
International application No. PCT/US 02/ 04772	FOR FURTHER ACTION See paragraphs 1 and 4 below International filing date <i>(day/month/year)</i> 15/02/2002
Applicant GENETICS INSTITUTE, INC.	

1. The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Catriona Cleere	RECEIVED LAHIVE & COCKFIELD ENTERED DOCKET DEPT. APR - 3 2003
INITIALS 		
RETRIEVED <i>1/8</i> FORWARDED <i>1/8 / 2003</i>		

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the International application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the International application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the International application is English, the letter must be in English; if the language of the International application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference GNN-028PC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 02/ 04772	International filing date (day/month/year) 15/02/2002	(Earliest) Priority Date (day/month/year) 16/02/2001
Applicant GENETICS INSTITUTE, INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
 - contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. **Certain claims were found unsearchable** (See Box I).

3. **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

National Application No
PCT/US 02/04772

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/395 A61K38/00 A61P37/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

MEDLINE, EPO-Internal, WPI Data, PAJ, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PERRIN P J ET AL: "Blockade of CD28 during in vitro activation of encephalitogenic T cells or after disease onset ameliorates experimental autoimmune encephalomyelitis." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD.: 1950) UNITED STATES 1 AUG 1999, vol. 163, no. 3, 1 August 1999 (1999-08-01), pages 1704-1710, XP002233476 ISSN: 0022-1767 page 1706 -page 1707 ---	1-7, 9-15, 17-23
Y	---	-/- 3,11,19

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

17 March 2003

31/03/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Wagner, R

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/04772

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TAN P ET AL: "Humanization of an anti-CD28 antibody using germline human antibody sequences" BLOOD, W.B. SAUNDERS, PHILADELPHIA, VA, US, vol. 96, no. 11 PART 1, November 2000 (2000-11), page 31A XP002177441 ISSN: 0006-4971 abstract ---	3,11,19
X	WO 94 28912 A (UNIV MICHIGAN ;US GOVERNMENT (US)) 22 December 1994 (1994-12-22) page 12 -page 13 ---	1-24
E	WO 02 051871 A (INST NAT SANTE RECH MED ;SOULILLOU JEAN-PAUL (FR); VANHOVE BERNARD) 4 July 2002 (2002-07-04) page 3 -page 9 ---	1,2,6, 8-10, 16-18, 22,24
A	WO 92 15671 A (CYTOMED INC) 17 September 1992 (1992-09-17) page 6 ---	5
A	WO 98 56401 A (APPLIED RESEARCH SYSTEMS ;TEPPER MARK (US); BLECHNER STEVEN (US);) 17 December 1998 (1998-12-17) page 13 ---	5
A	WO 92 00092 A (SQUIBB BRISTOL MYERS CO) 9 January 1992 (1992-01-09) claims 35-38 ---	1-24
A	SILVER P B ET AL: "Blockade of costimulation through B7/CD28 inhibits experimental autoimmune uveoretinitis, but does not induce long-term tolerance." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD.: 1950) UNITED STATES 1 NOV 2000, vol. 165, no. 9, 1 November 2000 (2000-11-01), pages 5041-5047, XP002233477 ISSN: 0022-1767 the whole document -----	1-24

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: not searched 5, 13, 21; seached in part 6-8, 14-16, 22-24

Claims 5, 13, 21 and corresponding subject-matter of the respective dependent claims 6-8, 14-16, 22-24 are not supported by the description (Article 6 PCT) and not sufficiently disclosed (Article 5 PCT) because the description does not disclose any "small molecules". On page 35 of the description a definition of the -expression "small molecule" is given (m.w. less than 1000 or 500). The description merely indicates that libraries of small molecules can be screened and leaves the skilled person with the undue burden of finding the small molecules that would block CD-28. Claims 6-8, 14-16 and 22-24 were searched only in regard to antigen-binding portions of antibodies directed against anti-CD28.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 02/04772

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-24 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound.
2. Claims Nos.: not searched 5, 13, 21; searched in part 6-8, 14-16, 22-24 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

National Application No

PCT/US 02/04772

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 9428912	A	22-12-1994	AU WO	7107794 A 9428912 A1		03-01-1995 22-12-1994
WO 02051871	A	04-07-2002	WO	02051871 A2		04-07-2002
WO 9215671	A	17-09-1992	EP JP WO	0575537 A1 6505396 T 9215671 A1		29-12-1993 23-06-1994 17-09-1992
WO 9856401	A	17-12-1998	AU AU EP JP WO US	743939 B2 8070698 A 0989858 A1 2002505673 T 9856401 A1 6337316 B1		07-02-2002 30-12-1998 05-04-2000 19-02-2002 17-12-1998 08-01-2002
WO 9200092	A	09-01-1992	CA EP JP JP WO US US	2086325 A1 0537293 A1 6508501 T 2002186486 A 9200092 A1 5521288 A 5580756 A		03-01-1992 21-04-1993 29-09-1994 02-07-2002 09-01-1992 28-05-1996 03-12-1996